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EXPERIMENTAL STUDIES

Hemodynamic Evaluation of a Chronically Implanted, Electrically Powered Left Ventricular Assist System: Responses to Acute Circulatory Stress

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Hemodynamic stress testing was performed in four calves with a chronically implanted left ventricular assist device consisting of a double-valved pump interposed between the left ventricular apex and the descending thoracic aorta. The device was powered either pneumatically (n = 1) or with a transcutaneous energy transmission system (n = 3). Hemodynamic evaluation (cardiac output and right and left ventricular and pulmonary and carotid artery pressures) was carried out at baseline and during all hemodynamically stressed states.

Atrial pacing and ventricular pacing to a heart rate of 140 beats/min resulted in no significant change in right or left heart filling pressures or cardiac output. Preload reduction with nitroprusside or transient inferior vena cava balloon occlusion resulted in a marked decrease in left ventricular pressure with preservation of mean arterial pressure. Phenylephrine administration resulted in a marked rise in mean arterial pressure with no change in cardiac output or filling pressure. Induction of ventricular fibrillation resulted in a decrease of mean left ventricular pressure to 11 ± 8 mm Hg, but mean arterial pressure was maintained at ≥50 mm Hg.

It is concluded that a multicomponent, implantable, electrically powered assist system is capable of maintaining a normal cardiac output under a wide range of loading conditions and chronotropic states. Although this device is clearly preload dependent, it is capable of maintaining normal systemic pressures during conditions of severe left ventricular dysfunction and circulatory collapse.

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Early studies by Bernhard et al. (1) demonstrated the clinical utility of long-term left ventricular bypass with the use of a pneumatically actuated, double-valved pump that was interposed between the left ventricular apex and the ascending thoracic aorta. Successful use of the system has been documented in calves for periods of up to 14 months. This assist system has also been successfully used for short-term hemodynamic support in selected patients after open heart surgery (2–5).

A goal of left ventricular assist device research has been the eventual development of a totally implantable, tether-free, electrically powered system for long-term implantation in ambulatory patients with irreversible left ventricular dysfunction. Effective utilization of such a device requires reliable long-term operation with the ability to respond appropriately to acute hemodynamic stresses, including abrupt changes in heart rate, rhythm, preload, afterload and native left ventricular function. This report describes the use of such a system in calves, employing a pusher-plate blood pump, energy converter and controller, all completely implanted and electrically actuated through a transcutaneous energy transmission system. The hemodynamic performance of the electrically powered system implanted in three healthy calves is described in response to acute circulatory stress, and compared with results in a fourth calf with a similar device driven by an external pneumatic power source.

Methods

Description of the Left Ventricular Assist System

The multicomponent ventricular assist system that has been developed is an electrically actuated device consisting of a pusher plate blood pump and Dacron-valved conduits coupled to a low speed torque motor (Thermedics). An internal, variable volume chamber attached to the motor assembly serves as a reservoir for air displaced during each pump cycle. Synchronization of the system with the [illegible] is

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provided by a controller/internal energy storage unit. A transcutaneous energy transmission system conducts electrical power to the motor across intact skin, eliminating the need for percutaneous tubes or wires with their attendant hazard of infection.

Blood pump and contiguous energy converter. The pusher-plate pump (maximal stroke volume 85 ml) and an integral electromechanical energy converter (weight 0.87 kg) are capable of ejecting a pulsatile flow (in vitro) of 10 liters/min (mean) at a maximal rate of 140 beats/min. The rigid pump housing and energy converter were fabricated from a titanium alloy, and contain a flexible, polyurethane diaphragm (biomer) that isolates one component from the other. Upward displacement of the diaphragm by the motor produces systolic ejection; diastolic filling occurs during passive recoil of the diaphragm. The diaphragm has a textured, fibrillar, blood-contacting surface (mat thickness of 350 μm) to attract and bind a thin fibrin-cellular coagulum. The internal surface of the adjacent pump housing is covered by a powdered metallurgy layer consisting of masses of interconnected titanium microspheres, each approximately 140 μm in diameter. This lining functions in a manner similar to the fibrillar diaphragm, and also attracts a fibrin-cellular coagulum (6).

The low-speed torque motor operates on a beat to beat basis and has only four moving parts. On receipt of an ejection signal, the rotor of the unit turns one revolution and stops (systolic ejection). The motor contains solid state electronic commutation, and a magnet mounted on the pusher-plate plus a sensor located in the center shaft of the rotor) permits monitoring of pusher-plate position. This electronic technique provides a measurement of stroke volume and plate velocity for monitoring the ventricular assist system performance.

Variable volume chamber. In the absence of an external vent (between the motor and the external environment), a chamber is used to maintain a constant gas volume within the motor during systolic ejection and diastolic filling. The chamber consists of a rigid backplate and a flexible (Biomer-Butyl elastomer) discoidal sac covered with Dacron velour fabric. The presence of a velour layer promotes formation of a thin capsule at the sac surface in contact with the visceral pleura (left lung). During ventricular assist system function, the chamber inflates with air as blood flows into the pump, and deflates into the motor section during synchronized ejection of blood. The fibrous capsule inhibits formation of thick pleural adhesions that could restrict motion of the chamber and limit pump function.

Control system/internal energy storage unit. The control unit is encased in a titanium housing and consists of three interconnected printed circuit boards, 3.8 cm in diameter. Ten nickel-cadmium batteries are included in the housing, forming a battery of 4.5-watt-hours (w-h) capacity to supply 8 W of power. The batteries constitute an emergency back-up capability for the ventricular assist system in the case of power failure, and have a discharge time in excess of 40 min.

Three operating modes are possible within the controller: synchronous counterpulsation, fixed volume asynchronous pumping and fixed rate operation. Synchronization of the device when implanted in patients is accomplished by detecting changes in pump fill rate, corresponding to the rate of descent of the pusher-plate (after ventricular systole). Electrocardiographic (ECG) signals are not monitored because of the inherent potential for fatigue-fracture of myocardial leads. In the calves used in this experimental model, the large stroke volume of the ventricle may lead to early filling of the device chamber, before completion of ventricular systole, thus disrupting the timing of counterpulsation. Therefore, ECG signals were used (in this experiment) to adjust timing of device ejection during synchronous counterpulsation. Device timing was also manipulated by means of the ECG to observe the effects of synchronous copulsation, when the native ventricle and the left ventricular assist device ejected simultaneously.

Transcutaneous energy transmission system. The transcutaneous energy transmission system consists of a power oscillator, a tuned, transcutaneous transformer and output power-conditioning circuitry. The oscillator converts direct current power from external batteries to alternating current 160 kHz. During pump function, AC current is conducted to a superficial primary coil on the external chest wall and inductively coupled to an implanted, subcutaneous, secondary coil. High frequency magnetic fields are capable of transmitting power through an unbroken layer of skin up to 1.5 cm in thickness and are approximately 75% efficient.

External battery capacity and power requirements. The external battery power source, carried in a body harness or belt, provides 10 h of pump function at a minimal flow rate of 7.0 liters/min, 120-mm Hg mean pressure. Blood flow of this magnitude constitutes a 5-W power drain. This power has added to it the 1.7 W necessary for implanted electronics and internal battery charging. Additional small power losses are incurred in transferring energy across the intact skin, resulting in a total power requirement of 7.8 W (10 h of operation). Batteries must be replaced with an alternate unit every 8 to 10 h and recharged with use of a recharger unit powered from a conventional wall outlet.

Surgical Implantation Method (Fig. 1)

The pusher-plate pump, controller and other components of the electrical ventricular assist system were positioned through a left thoracotomy incision and a separate left subcostal (abdominal) incision. The pump housing and controller were attached with sutures to the 9th and 10th ribs (subdiaphragmatic location), and the secondary TET coil was implanted in a subcutaneous pocket adjacent to the 9th vertebra posteriorly to permit induction of electrical AC current.

Two bioprosthetic valved conduits (inflow and outflow), coupled to the blood pump, were connected to the left ventricular apex and descending thoracic aorta (end to side

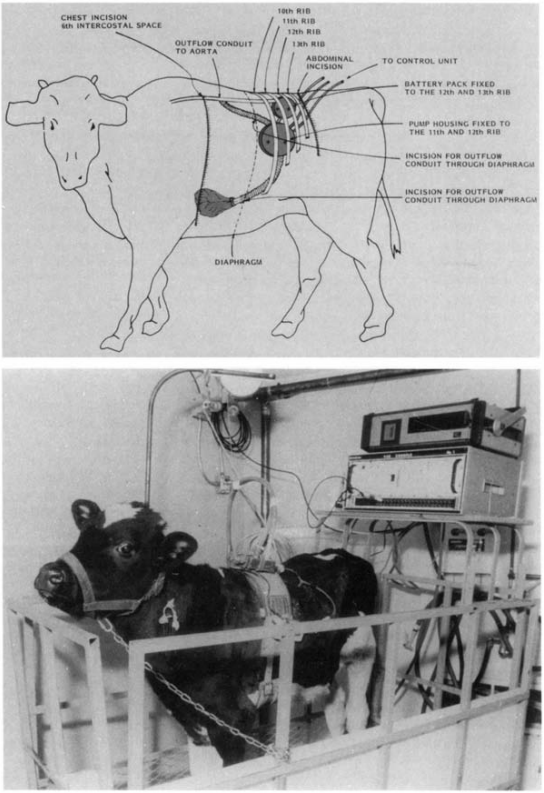

Figure 1. Illustration of left ventricular assist device components and surgical implantation in schematic form (**top**) and in intact calf (**bottom**). See text for details.

anastomoses) through short incisions in the left hemidiaphragm (Fig. 1). Maximal blood flow to the pump was attained by advancing the titanium inflow cannula into the left ventricular chamber to the base of the posterolateral papillary muscle (mitral valve). This position prevented encroachment on the lumen of the cannula by either the left ventricular free wall or the interventricular septum. The variable volume chamber, connected by a cable to the motor housing, was placed in the left pleural space, and fixed in position with sutures (fifth and sixth ribs).

Hemodynamic Stress Testing of the Left Ventricular Assist System

Study animals. After surgical implantation of the left ventricular assist system, calves recovered uneventfully with routine postoperative care. The system was activated immediately after implantation and kept continuously active thereafter. The left ventricle of calves receiving the assist system was normal and not rendered dysfunctional, and the assist system functioned by filling at the normal left ventric-

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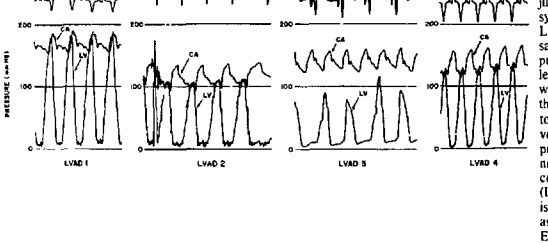


Figure 2. Left ventricular and arterial pressures in the four calves with a chronically implanted left ventricular assist device (LVAD), illustrating the different modes of operation. In mode 1 (LVAD 1), synchronous copulsation, the pump ejects in conjunction with left ventricular (LV) systole. In mode 2 (LVAD 2 and LVAD 4), synchronous counterpulsation, the stroke volume of the pump is ejected just after the peak of left ventricular systolic pressure, with the pump generating pressure throughout most of ventricular diastole. In mode 3 (LVAD 3), fixed volume asynchronous pulsation, the pump operates at a fixed rate and is not coordinated with left ventricular contraction. Note that in calf 3 (LVAD 3), total circulatory support is provided by the left ventricular assist device. CA = carotid artery; ECG = electrocardiogram.

ular preload (see Results). Four calves with an implanted left ventricular assist system, powered either pneumatically (n = 1) or with a transcutaneous energy transmission system (n = 3), were studied with right and left heart catheterization a mean of 4 ± 2 weeks after surgical implantation. At the time of study, the average weight of the calves was 102 ± 3 kg. In all animals, surgical cutdown of the right internal jugular vein and right carotid artery was performed with placement of 8F sheaths in both vessels. Right heart catheterization was performed with a 7F balloon-tipped Swan-Ganz catheter advanced to the pulmonary artery. A 7F pigtail catheter instrument with a 2F Millar micromanometer catheter was used for left heart catheterization and catheterization through the inflow conduit, pump and outflow conduit of the left ventricular assist system.

Hemodynamic stresses. Atrial and ventricular pacing were performed with a 7F USCI bipolar pacer. Inferior vena cava occlusion was performed with placement of a 40-mm occlusion balloon in the inferior vena cava. Changes in preload and afterload were achieved with administration of nitroprusside and phenylephrine. Pump function was also examined during spontaneous or induced ventricular fibrillation. Results are reported as mean values ± SD.

Results

Baseline hemodynamic evaluation. The left ventricular assist pumps were operated in one of three modes during these experiments (Fig. 2). In mode 1, synchronous copulsation, the pump ejects in conjunction with ventricular systole. In mode 2, synchronous counterpulsation, the stroke volume of the pump is ejected just after the peak of left ventricular systolic pressure, with the pump generating pressure throughout most of ventricular diastole. In mode 3, fixed volume asynchronous pulsation, the pump operates at a fixed rate and is not coordinated with left ventricular contraction.

Baseline right and left heart catheterization was performed in the four calves (average weight 102 ± 3 kg). In the first calf, in which the left ventricular assist device was powered by an external pneumatic pump, right atrial pressure was 3 mm Hg, right ventricular pressure 25/2 mm Hg, pulmonary artery pressure 25/12 (mean 15) mm Hg, mean pulmonary capillary wedge pressure 6 mm Hg, left ventricular pressure 173/6 mm Hg, and systemic pressure 182/155 (mean 162) mm Hg. Rest cardiac output was 7.5 liters/min and systemic vascular resistance and pulmonary vascular resistance were 1,696 and 96 dynes·s·cm^{-5}, respectively.

In Calves 2, 3 and 4, the left ventricular assist device was an electrically driven device with a transcutaneous power source. The average baseline hemodynamics in these three calves included a mean right atrial pressure of 8 mm Hg, right ventricular pressure 34/8 mm Hg, pulmonary artery pressure 34/17 (mean 24) mm Hg, mean pulmonary capillary wedge pressure 14 mm Hg, left ventricular pressure 107/15 mm Hg and systemic pressure 143/108 (mean 120) mm Hg. Rest cardiac output was 8.4 liters/min and systemic and pulmonary vascular resistance values were 1,067 and 96 dynes·s·cm^{-5}, respectively.

Catheterization of the left ventricular assist device in all four calves revealed a physiologic gradient across the distal outflow conduit, with a mean 38-mm Hg gradient in systolic pressure from the pump chamber to outflow vessel (aorta) (Fig. 3). Note that during diastole, a negative diastolic pressure is recorded that may be responsible for preferential filling of the left ventricular assist device (versus the left ventricle).

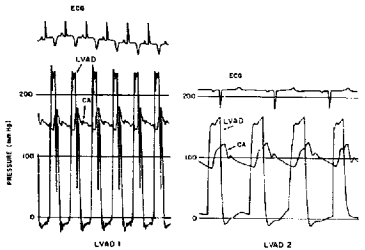


Figure 3. Demonstration of pressure gradient from the left ventricular assist device (LVAD) pump chamber to the aorta (here equal to the carotid artery [CA]) for modes 1 and 2. The average peak systolic gradient for the four calves was 38 mm Hg. Note that a negative pressure is generated by the left ventricular assist device during diastole, which may be responsible for preferential filling of the left ventricular assist device (versus the left ventricle).

Inferior vena cava occlusion. Marked reduction in ventricular preload was successfully achieved in the three calves with the electrical left ventricular assist device by transient occlusion of the inferior vena cava (Fig. 4). At peak inflation, left ventricular systolic pressure decreased to an average of 14 ± 25 mm Hg, a preload dependence of the pump system is illustrated by the progressive decrease in arterial blood pressure during inferior vena cava obstruction. However, arterial pressure stabilized at 97 ± 21 / 52 ± 12 mm Hg. The marked effect of inferior vena cava occlusion on left ventricular pressure suggests that the reduced venous return arriving at the left atrium is preferentially shunted to the left ventricular assist device, which has the capability of generating diastolic suction (Fig. 3).

Nitroprusside administration. This resulted in a 60-mm Hg decrease in mean systemic arterial pressure from baseline. Cardiac output decreased from 7.5 to 4.8 liters/min in the calf with the pneumatic device and from 8.4 to 6.6 liters/min in two calves with the electrical device.

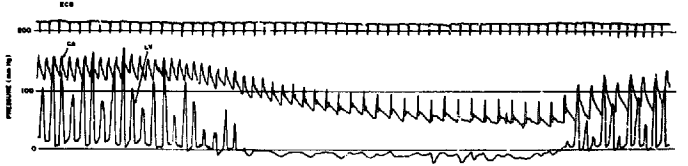
Atrial and ventricular pacing. Successful atrial pacing was performed in the four calves, with a mean increase in heart rate to 140 beats/min. With both the pneumatic and the electrical devices, no significant difference was noted in pulmonary artery pressure, pulmonary capillary wedge pressure, carotid artery pressure, mean arterial pressure, thermodilution cardiac output, systemic vascular resistance and pulmonary vascular resistance during pacing tachycardia. The contribution of the left ventricular assist system continued to be substantial, as inferred from the persistent support of aortic pressure higher than left ventricular systolic pressure. Similar results were noted with ventricular pacing.

Phenylephrine administration. Administration of phenylephrine resulted in a 35 to 60 mm Hg increase in peak systolic and mean arterial pressures with an accompanying increase of 6 mm Hg in mean pulmonary capillary wedge pressure in the four calves. Peak systolic aortic pressure exceeded left ventricular pressure in all cases, with aortic diastolic pressure matching left ventricular systolic pressure in the three calves with the electrical device, again indicating that the left ventricular assist device was generating systemic pressure.

Induction of ventricular fibrillation. In three calves, hemodynamic measurements were made after 20 min of ventricular fibrillation. Examples of support of systemic arterial pressure by the left ventricular assist device during ventricular fibrillation are shown in Figure 5. Note the marked effect of mean left ventricular pressure on the ability of the pump to generate aortic systolic and diastolic pressures, implying that even in ventricular fibrillation volume loading could restore an effective cardiac output.

Autopsy. Animals were killed at the end of the hemodynamic protocol. There was no evidence of thromboembolism within the left ventricular assist device or its connections with the heart and aorta, nor were there any other complications associated with the device or its electrical control system.

Figure 4. Preload dependence of the left ventricular assist device is demonstrated by inferior vena cava balloon occlusion in Calf 3 (asynchronous mode). Note the maintenance of carotid artery (CA) pressure at 90/50 mm Hg despite the complete abolition of left ventricular (LV) pressure. The marked effect of inferior vena cava occlusion on left ventricular pressure suggests that the reduced venous return arriving at the left atrium is preferentially shunted to the left ventricular assist device, which has the capability of generating diastolic suction (see Fig. 3).



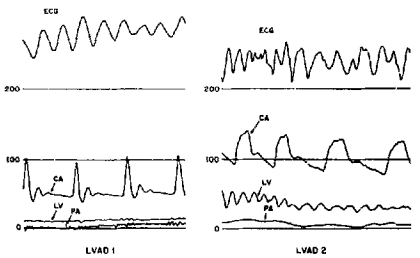


Figure 5. Left ventricular assist device (LVAD) support during ventricular fibrillation in two experiments (LVAD 1 and LVAD 2). Note the preservation of carotid artery (CA) pressure during loss of left ventricular (LV) pressure. Pulmonary artery (PA) pressure is also shown. At higher right heart, pulmonary artery and left ventricular pressures (right panel), the left ventricular assist device is able to produce a normal arterial blood pressure.

Discussion

A significant limitation of this study is the small number of experimental subjects, each of which was subjected to multiple interventions during the course of hemodynamic study. Statistical analysis of the differences in hemodynamic variables is prevented by the small number of animals tested, but the combined cost of approximately $100,000 per experiment (for the animal, housing, the left ventricular assist device, hemodynamic testing and other factors) precluded a larger study. Within the context of this limitation the electrical system described here has the advantage of being totally implantable and tether free, to permit permanent implantation in ambulatory patients with irreversible left ventricular dysfunction.

Previous studies. Early studies by Bernhard et al. (1) demonstrated that a temporary, pneumatic double-valved device, interposed between the ventricular apex and aorta, can augment or replace native cardiac output while reducing left ventricular peak pressure and myocardial energy consumption. That early system suffered from the disadvantage of requiring an external pneumatic control system to drive the implanted device by way of a percutaneous tube. Investigation of the use of assist systems to aid left heart pumping dates back to the 1960s (7), with most initial designs comprising a paracorporeal pump connected by catheters to the left atrium and descending aorta, and employing an extracorporeal pneumatic driving unit. Many current implantable pump systems now use the left ventricular apex as the site of the pump inflow port.

Pennock et al. (8) in 1979 noted that experimental acute infarct size in dogs with left ventricular assist device placement using ventricular cannulation was significantly less than that in control animals without an assist device. The physiologic advantages of a left ventricular assist system were also demonstrated by Mickleborough et al. (9), using a canine model of left ventricular failure caused by normothermic ischemic arrest. A comparison of the left ventricular assist device versus a combination of inotropic drugs and intraaortic balloon counterpulsation showed satisfactory hemodynamic support in each case, but the heart of those dogs treated with the left ventricular assist device had significantly less decrease in compliance and systolic function and less myocardial necrosis on histologic examination. The electrically powered, chronically implanted device profiled in the present report was able to provide continued circulatory support despite a variety of acute hemodynamic stresses, and its performance was comparable to that of a device that used an external pneumatic pump as power source. Moreover, as opposed to dogs, the large animals (average weight 102 ± 3 kg) used in our study have a circulatory requirement equal to or greater than those of humans.

Baseline hemodynamic values. At baseline, hemodynamic variables were notable for systemic diastolic hypertension in these calves after general anesthesia and instrumentation. Total cardiac output, reflecting the combined output of the native heart and the assist device, was approximately 8 liters/min in the unstressed state. Peak systolic left ventricular pressure was at or below mean aortic pressure, suggesting that the majority of circulatory support was being furnished by the left ventricular assist device. The left ventricular pressure was reduced most dramatically in comparison with aortic pressure when the pump was operated in the asynchronous mode as seen in Figure 2 for Calf 3 (electrically powered). This finding is consistent with the work of Nakamura et al. (10), who noted that mean aortic pressure and total flow were highest in a 1:1 synchronous pumping mode, whereas asynchronous pumping was more useful in reducing mechanical work of the left ventricle.

Atrial or ventricular pacing and phenylephrine. Pacing at rates up to 140/min produced a slight decline in systemic arterial and left ventricular pressures, with only small changes in pulmonary capillary wedge pressure and cardiac output. While in the synchronous mode, both the electrical and the pneumatic devices could track appropriately 1:1 at an atrial paced rate of 140/min. Afterload augmentation with phenylephrine appropriately elevated systemic arterial pressure, but cardiac output and left ventricular end-diastolic

pressure were unchanged. This observation suggests continued adequate forward ejection by the pump despite an acute rise in afterload, with minimal evidence of retrograde transmission of elevated pressure.

Nitroprusside administration and inferior vena cava occlusion. Nitroprusside markedly lowered left ventricular and systemic arterial pressures, as expected. Left ventricular end-diastolic pressure decreased as did cardiac output despite appropriate reflex tachycardia. This diminution in flow underscores the preload dependency of the left ventricular assist device; because the pump chamber accepts blood from the left ventricle, pump filling is critically sensitive to reduction in left ventricular filling pressure. This preload dependency was demonstrated even more dramatically by inferior vena cava balloon occlusion. Systemic arterial pressure decreased rapidly but was maintained at an average of 97/52 mm Hg, whereas left ventricular pressure was virtually obliterated (Fig. 4). This stabilization of systemic arterial pressure despite the lack of significant developed left ventricular pressure suggests that although both chambers are highly preload dependent, the left ventricular assist device pump may fill preferentially (to the left ventricle) when preload is reduced.

Ventricular fibrillation. During ventricular fibrillation, the support of the circulation by the pneumatic and electric left ventricular assist device were comparable, with systemic arterial pressure ranging from 85/50 to 130/90 mm Hg (Fig. 5) and cardiac output from 2.5 to 2.7 liters/min despite the virtual absence of developed left ventricular pressure. These findings again demonstrate the limitations of preload dependency for these devices which assist only the left ventricle. While the continued evacuation of the left ventricle by the left ventricular assist device and forward ejection of blood into the systemic arterial circulation limit the increase in left-sided filling pressures and pulmonary congestion, coexistent right ventricular failure prevents optimal filling of the left ventricular assist device pump chamber from the left ventricle. However, the ability of this device to maintain adequate perfusion pressure and a low cardiac output in these states of minimal or absent ventricular function indicates that some degree of effective filling must still occur, with negative pressure developed by the left ventricular assist device a potential source of augmented pump filling in these conditions. Limitation of pulmonary congestion and right ventricular dilation was documented by postmortem examination in these animals, which died from irreversible ventricular fibrillation induced as part of the study protocol (electrical defibrillation was not possible in these closed chest animals because of the high electrical resistance of their thick hides). Some pulmonary congestion and right ventricular dilation were seen in these calves, but they were minimal. The influence of left ventricular assist devices on right ventricular function has been shown to be favorable in recent studies (11,12).

Clinical implications. The clinical benefits of mechanical left ventricular assistance have been shown by many investigators who have assessed its role in the management of cardiogenic shock after aortocoronary bypass or valve replacement surgery (2–5,13–15), in acute fulminant myocarditis (16) and as a "bridge" to cardiac transplantation (17–20). Thromboembolic complications of left ventricular assist devices are rare (13,19), particularly with the use of a textured blood-contacting surface that promotes neointimal development (20), as in the device utilized in the present study.

Conclusions. A totally implantable, electrically powered left ventricular assist system is capable of maintaining a normal cardiac output under a broad range of loading conditions in a large animal (average weight 102 ± 3 kg) with circulatory requirements similar to those of humans. The function of the tether-free electrical left ventricular assist device evaluated here in response to acute hemodynamic stress is wholly comparable to that of a device using an external pneumatic pump as power source. Although clearly preload dependent, the device can effectively support systemic arterial pressure at near normal levels during conditions of severe hemodynamic stress and circulatory collapse.

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